REMARKS

Status of the Claims

Claims 95-149 were pending. Claims 105-112, 114-117, 122, 123, 132, 133, 142 and 143 were asserted by the Office Action mailed 1/12/06 to be withdrawn as drawn to non-elected species. However, as discussed below, Applicants respectfully submit that the species election dated 1/20/2004 was mis-interpreted and assert that the presently pending claims are consistent with the actual species election, a copy of which is attached herewith for convenience, along with a copy of the corresponding restriction requirement. Claims 101-104, 109, 111-112, 114, 116-125 and 128-149 are canceled herein. Claims 95-100, 105, 107, 108, 113, 115 and 126-127 are amended herein to further clarify the claimed subject matter. Support for the amendments is discussed below in the section on written description support. Applicants submit that no new subject matter is added by amendment. Applicants respectfully assert that claims 95-100, 105-108, 110, 113, 115 and 126-127 should be considered as presently pending. However, to comply with the Office Action of August 9, 2006, the claim designations have been changed to reflect the designations indicated in the Office Action mailed 1/12/06. Reconsideration of the Examiner's withdrawal of claims is requested.

Species Election of 1/20/2004

Attached hereto are copies of the restriction requirement mailed 12/18/2003 and response to restriction requirement, dated 1/20/2004. The Action (mailed 1/12/2006) at Paragraph 3 asserts that, "Applicant's election of the species antibody of SEQ ID No 2 and 4 in the reply filed on 1/20/2004 is acknowledged." Applicants respectfully traverse.

The restriction requirement mailed 12/18/03, stated that, "This application contains claims directed to the following patentably distinct species of the claimed invention. The various different nucleic acids encoding a particular antibody. For example, the nucleic acid encoding the antibody of SEQ ID NO:2 and 4, or the nucleic acid encoding the antibody of claim 111, etc). These are different antibodies with different sequences. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable."

By use of the phrase, "for example," the restriction requirement made clear that the species to be elected were not limited to "the antibody of SEQ ID NO:2 and 4," or "the antibody of claim 111." Rather, the choice of the disclosed species was left to the Applicants to select.

In the response dated 1/20/04, "Applicant hereby provisionally elects claims directed to a polynucleotide sequence encoding an antibody that contains one or more CDRs from SEQ ID NOS:2 and/or 4 (amino acid sequences of the variable light and heavy chain murine LL2 monoclonal antibody) or components of these antibodies, such as individual CDRs, light chain variable regions or heavy chain variable regions containing these CDRs."

Thus, the species elected was the polynucleotide encoding an antibody or fragment thereof containing one or more CDRs from SEQ ID NO:2 and/or SEQ ID NO:4. Applicants respectfully submit that all pending claims read on the elected species. Further, Applicants submit that the species was a proper species for election. All embodiments of the elected species share a common structural feature – they contain one or more CDRs selected from SEQ ID NO:2 and/or SEQ ID NO:4. Further, this common structural feature is related to the function of the encoded antibody or fragments thereof – that of binding to the same antigen as the murine LL2 antibody from which the CDR sequences were obtained. It is well known in the art that antigen-binding specificity is determined by the CDR sequences of antibodies. The Office Action of 1/12/06 explicitly recognized this fact, stating that, "The claims reading on CDRs derived from the elected species have been included as part of the elected species." All presently pending claims read on CDRs derived from SEQ ID NO:2 and/or SEQ ID NO:4.

Non-statutory Double Patenting Rejection

The claims were rejected on the ground of non-statutory obviousness-type double patenting over claims 25-27 of U.S. Patent No. 6,187,287. Applicants respectfully traverse. Claims 25-27 of U.S. Patent 6,187,287 are drawn to DNA sequences or vectors encoding chimeric LL2 antibodies or fragments thereof (cLL2), "wherein said cLL2 mAb retains substantially the B-lymphoma cell and leukemia cell targeting and cell internalization characteristics of said mLL2 mAb." Applicants respectfully submit that claims 25-27 of U.S. Patent 6,187,287 are patentably distinct from the instant claims, which do not recite the limitations cited in the preceding sentence.

Rejection of Claims Under 35 USC 112, 1st Paragraph

The claims were rejected under 35 USC 112, 1st paragraph for failure to comply with the written description requirement. The Office Action of 1/12/06 asserted that, "There is no support in the specification as originally filed for the nucleic acids of claims 95-100." Applicants respectfully traverse the assertion.

Concerning claims 95-100, the claims as amended concern isolated polynucleotides encoding humanized or chimeric antibody fragments comprising the light chain CDR1, CDR2 and/or CDR3 or the heavy chain CDR1, CDR2 and/or CDR3. Applicants submit there is ample written description support for those claims.

First, the Office Action of 1/12/06 at Paragraph 15 states that, "All of the instant polynucleotide claims are considered 'open' and therefore encompass the nucleic acids encoding the chimeric LL2 antibody." This is consistent with the use of "comprising" in the instant claims.

Applicants submit that Figures 5A and 5B disclose isolated polynucleotides encoding humanized or chimeric antibody fragments comprising CDR1, CDR2 and/or CDR3 of the LL2 light chain and/or CDR1, CDR2 and/or CDR3 of the LL2 heavy chain. The skilled artisan, viewing Figure 5, would clearly conclude that Applicants were in possession of isolated polynucleotides encoding humanized or chimeric antibody fragments comprising CDR1, CDR2 and/or CDR3 of the LL2 light chain and/or CDR1, CDR2 or CDR3 of the LL2 heavy chain as of the priority date of the instant application.

Further, Figure 6 and Example 3 of the instant application show that the humanized VH sequence was produced in the form of two polynucleotides – identified as "oligo A" and "oligo B." Example 3 discloses that "oligo A" extended from nucleotides 24 to 172 of the complementary hLL2 VH domain, while "oligo B" extended from nucleotides 180 to 320 of the hLL2 VH. Examination of FIG 5B shows that oligo A encoded the amino acid sequence comprising CDR1 and part of CDR2 of the heavy chain hLL2, while oligo B encoded the amino acid sequence comprising CDR3 and part of CDR2 of the heavy chain hLL2. The Specification at page 11, line 15 to page 12, line 17, page 26, lines 26-28, and page 27, lines 1-24 discloses that the nucleic acid encoding the light chain variable sequence of hLL2 was also synthesized in 2 segments, the first encoding CDR1

and part of CDR2 and the second encoding CDR3. Such polynucleotides are of use, for example, to construct an intact humanized or chimeric LL2 antibody or a fragment thereof. The cited passages and oligos A and B explicitly disclose "nucleic acids encoding variable heavy chain and or variable light chains wherein said nucleic acids encode less than all of the CDRs found in the LL2 heavy and or light chain variable chain regions," for which the Office Action of 1/12/06 at Paragraph 12 asserted a lack of written description support.

The skilled artisan, reading the Specification as cited above, would conclude that Applicants were in possession of polynucleotides encoding humanized or chimeric antibody fragments comprising CDR1, CDR2 and/or CDR3 of the light and/or heavy chains of LL2 as of the priority date of the instant application.

Claim 113 also finds support in the Specification in Figures 5A and 5B and in Examples 3 and 4, which clearly describe the construction of polynucleotides and vectors encoding humanized and chimeric VH and VL sequences comprising CDR1, CDR2 and CDR3 of the light and heavy chains of LL2. Thus, the skilled artisan reading the specification would conclude that Applicants were in possession of the subject matter of Claim 113 as of the instant priority date.

Applicants further submit that there is support in the Specification for amended claims 105-110, which depend from claim 113 and therefore concern isolated polynucleotides encoding humanized or chimeric antibodies or fragments thereof, comprising CDR1, CDR2 and CDR3 of the light and heavy chain variable sequences of LL2. As acknowledged in the Office Action of 1/12/06 at Paragraph 12, "The specification discloses chimeric LL2 antibody or humanized LL2 antibody wherein said nucleic acids encode all of the CDRs derived [from] the murine LL2 antibody and contain human FR regions (humanized) or the FR regions of the murine LL2 antibody." Thus, even the Office Action of 1/12/06 demonstrates that claim 113 is fully supported by the Specification and that written description support also exists for dependent Claims 105 and 110.

With respect to the FR substitutions of claims 106-108, there is disclosure throughout the Specification in support, including at least Example 1, which discloses a glutamine for valine substitution at amino acid position 5 and Example 8, which discloses substitution of glutamine for asparagine at residue 18 in FR1.

The subject matter of amended Claim 107 is supported in the Specification at least at page 10, line 17 to page 11, line 13. Page 2, lines 22-34 of the Specification identifies CD22 as the LL2-binding antigen on B-cells. Page 5, lines 2-19 of the Specification support that the cLL2 and hLL2 mAbs retain the antigenic specificity of the mouse LL2 antibody. There is ample support in the Specification that the CDRs incorporated into hLL2 and cLL2 were derived from the murine LL2 mAb.

Expression vectors comprising the claimed polynucleotides (Claim 126) are disclosed in the Specification at least at Example 3 and Figure 3. The Office Action of 1/12/06 at Paragraph 12 notes that, "The specification discloses the use of 'mammalian expression cells'" (Claim 127).

Priority to Parent Applications

Paragraph 13 of the Office Action of 1/12/06 asserts that the instant application is not entitled to priority to the parent applications, "for the same reasons that said claims constitute new matter." Applicants submit that withdrawal of the new matter rejection should also result in the granting of the claimed priority. It is noted that the instant application is one of a series of continuations (not continuations-in-part) that include all of the parent applications to which priority is claimed. Therefore, the disclosure of the instant application is identical to that of the parent applications and, if written description support is found for the amended claims in the instant application, then priority to the parent applications should be granted, based on the same written description support.

Rejection of Claims Under 35 USC 102(b)

The claims were rejected under 35 USC 102(b) as anticipated by Leung et al. (US Patent 5,789, 554). Applicants respectfully traverse.

Applicants note that the '554 patent issued from USSN 08/690,102, which was the grand-parent of the instant application and to which priority should properly be granted, as discussed above. Further, if Leung et al. discloses each and every element of the presently claimed invention, as required to support a rejection under 35 USC 102, then priority to the application of Leung et al. should properly be granted, as that application would then support the instant claims. If Leung et al.

fail to disclose each element of the pending claims, such that the priority claim is not proper, then rejection under 35 U.S.C. 102 over Leung et al. is improper and should be withdrawn,.

Rejection of Claims Under 35 USC 103

The claims were rejected under 35 USC 103(a) as obvious over Goldenberg et al., in view of Morrison et al., Cabilly et al, Boss et al., Orlandi et al. and Huston et al. (US Patent 5,258,498). The Office Action of 1/12/06 states that, "Goldenberg et al. teach the murine LL2 monoclonal antibody and hybridoma producing said antibody." The Office Action of 1/12/06 asserts that it would have been obvious to apply the methods of Morrison et al, concerning chimeric antibody production, to the monoclonal antibody LL2 disclosed in Goldenberg to produce chimeric or humanized LL2 antibodies or fragments.

Applicants respectfully traverse. There is no disclosure in Goldenberg et al. of the CDR sequences used to construct the claimed chimeric or humanized LL2 antibodies. Nor was the LL2 antibody publicly available as of the instant application's filing date. Thus, without either the CDR sequences used or a source of the mouse LL2 mAb, the skilled artisan would have had no way to construct the claimed humanized or chimeric LL2 antibodies or fragments thereof, which depend on the incorporation of LL2 CDR sequence. Attached herewith is a Declaration of Goldenberg, of record in this application, stating that the expression vectors encoding the hLL2 light and heavy chain variable sequences were not deposited until October 8, 2002, well after the December 22, 2000, filing date of the instant application. As discussed in the attached Declaration of Hansen, prior to 2002, the cloned vectors were maintained in the Department of Cellular and Molecular Biology at Immunomedics, Inc., where they were not publicly available.

Since neither the CDR sequences nor the LL2 mAb were publicly available as of the instant filing date, let alone the instant priority date, the skilled artisan would have had no reasonable expectation of success in making and using the claimed invention. Reconsideration and withdrawal of the rejections are respectfully requested.

Conclusion

For the reasons stated above, Applicant submits that the claims as amended are in condition for allowance and requests withdrawal of the rejections.

Respectfully submitted,

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